

Amendments to the Claims:

Claim 27 is amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented. The text of all claims presently under examination is presented below in the listing of claims, and all claims are presented with an appropriate defined status identifier.

Detailed and Complete Listing of Claims:

- 1-23. (Canceled).
24. (Previously Presented) A method of making a mammalian cell having a mismatch repair deficiency phenotype, comprising inactivating the mismatch repair system of the mammalian cell by disrupting both copies of a gene essential for mismatch repair.
- 25-26. (Canceled).
27. (Currently Amended) The method of claim 26 24, wherein the gene essential for mismatch repair is a mammalian *Msh2* gene or a mammalian homologue of a *mutL* gene.
28. (Previously Presented) The method of claim 27, wherein the gene essential for mismatch repair is a mammalian *Msh2* gene.
- 29-32. (Canceled).
33. (Previously Presented) A diploid mammalian cell made by the method of claim 24, wherein both *Msh2* alleles are inactivated and the cell is a *dMsh2-9* cell.
34. (Withdrawn) A method for stably incorporating through homologous recombination a donor DNA molecule into the genome of a mammalian recipient cell that has a mismatch repair deficiency phenotype, comprising transforming the recipient cell having a mismatch repair deficiency phenotype with a donor DNA molecule that is obtained from a donor cell, wherein the donor DNA molecule is stably integrated into the genome of the recipient cell through homologous recombination with a homologous recipient DNA molecule, and wherein the sequence of the donor DNA molecule is not identical with the sequence of the homologous recipient DNA molecule.
35. (Withdrawn) The method of claim 34, wherein the nucleotide sequence of the donor DNA molecule diverges from the nucleotide sequence of the homologous DNA molecule in the recipient cell by about 0.6% to about 5%.
36. (Withdrawn) The method of claim 34, wherein the nucleotide sequence of the donor

DNA molecule diverges from the nucleotide sequence of the homologous DNA molecule in the recipient cell by about 0.6% to about 30% in the region where homologous recombination can take place.

37. (Withdrawn) The method of claim 34, wherein the mammalian recipient cell is an embryonic stem cell or a germ line cell.

38. (Withdrawn) The method of claim 34, wherein the mammalian recipient cell is obtained from a cell line that is cultured *in vitro*.

39. (Withdrawn) The method of claim 34, wherein the mammalian recipient cell is obtained from an organ of a mammal.

40. (Withdrawn) The method of claim 34, wherein at least one of the nucleotide base or base pairs in the donor DNA is modified *in vitro* prior to transformation.

41. (Withdrawn) The method of claim 40, wherein the modification is a point mutation, an insertion of base pairs, or a deletion of base pairs from the donor DNA molecule, and wherein the modified donor DNA molecule diverges from the nucleotide sequence of the homologous DNA molecule in the recipient cell by about 0.6% to about 5%.

42. (Withdrawn) The method of claim 40, wherein the modification is a point mutation, an insertion of base pairs, or a deletion of base pairs from the donor DNA molecule, and wherein the modified donor DNA molecule diverges from the nucleotide sequence of the homologous DNA molecule in the recipient cell by about 0.6% to about 30% in the region where homologous recombination can take place.

43. (Withdrawn) The method of claim 34, wherein the donor DNA molecule is a chromosomal DNA fragment that is inserted into a YAC or cosmid vector.

44. (Withdrawn) The method of claim 34, wherein the donor DNA molecule is a double-stranded oligonucleotide 10-100 bases in length, and wherein the nucleotide sequence of the donor DNA molecule diverges from the nucleotide sequence of the homologous DNA

molecule in the recipient cell by at least one base pair, but no more than 5% of all base pairs.

45. (Withdrawn) The method of claim 34, wherein the donor DNA molecule is a single - stranded oligonucleotide 10-100 bases in length, and wherein the nucleotide sequence of the donor DNA molecule diverges from the nucleotide sequence of the homologous DNA molecule in the recipient cell by at least one base, but no more than 5% of all bases.

46. (Withdrawn) The method of claim 34, wherein the donor DNA molecule comprises a selectable marker gene flanked by two sequences, wherein one flanking sequence has at least 95% sequence identity to the corresponding sequence of the recipient DNA molecule and the other flanking sequence comprises a repetitive sequence.

47. (Withdrawn) The method of claim 46, wherein the repetitive sequence is a long interspersed element (LINE) or a short interspersed element (SINE).

48. (Withdrawn) A method of making a transgenic animal, comprising (a) inserting a genetically modified stem cell prepared according to the method of claim 34 into a blastocoel, (b) implanting the blastocoel into a womb of a female host animal to make the female animal pregnant, and (c) carrying the pregnancy to term to obtain a viable transgenic animal.

49. (Withdrawn) A transgenic animal made by the method of claim 48.